## PATENT COOPERATION TREATY

To: OA. DECONTI CAHIVE & COCKPIELD, LIP 23 STATE STREET BOSTON, MA 62109  WRITTEN OPINION THE PC INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)  Date of mailing (daymonth/year)  1 8 MAY 2005  Applicant's or agent's file reference  FUL-045CP2PC International application No. International filing date (day/month/year)  Profit Vold/26641  10 30 November 2004 (03.11.2004)  12 Thernational Patient Classification (IPC) or both national classification and IPC  PC(TV.00476641  12 30 November 2004 (03.11.2004)  13 November 2003 (03.11.2003)  14 Thernational Patient Classification (IPC) or both national classification and IPC  PC(TV.007K 1/00; C12N 1585 and US C1: 530/4/02; 435/325  Applicant  PRESIDISM AND PELLOWS OF HARVARD COLLEGE  1. This opinion contains indications relating to the following items:  Box No. II Basis of the opinion  Box No. II Priority  Box No. IV Lack of unity of invention  Box No. V Reasoned statement under Rule 43bis. 1(a)(i) with regard to novelty, inventive step or industrial applicability epichelosis and explanations supporting such statement  Box No. VI Certain documents cited  Box No. VI Certain defects in the international application  Box No. VII Certain defects in the international application  Eox No. VII Certain observations on the international application  2. FURTHER ACTION  If a demand for international preliminary examinary examination is made, this opinion will be consistered to be a written opinion of the International Preliminary Examining Authority ("IPRA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPRA and the chosen IPA has notified the International Bureau under Rule 66.104(7) that writing opinion of poinion of the little opinion is, as provided above, considered to be a written opinion of the opinion of form PCT/ISA/220.	om the	ONAL SPARCE	ING AUTH	ORITY						
WRITTEN OPINION OF THE BOSTON, MA 02109  WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY  (PCT Rule 43bis.1)  Date of maiting (alaymonth/year)  PERCENTER ACTION See paragraph 2 below  HU-04SCP2PC  International application No. International Biling date (alaymonth/year)  PCT/US04/36641  103 November 2004 (03.11.2004)  30 November 2003 (03.11.2003)  Tatemational Patent Classification (IPC) or both national classification and IPC  PC(T): COTK 1000, C12N 1585 and US Cl.: 530/402; 435/325  Applicant  PRESIDENT AND FEILOWS OF HARVARD COLLEGE  1. This opinion contains indications relating to the following items:  Bax No. II Basis of the opinion  Box No. IV Lack of unity of invention  Box No. Va. Reasoned statement under Rule 43bis.1(c)(i) with regard to novelty, inventive step are industrial applicability; citetions and explanations supporting such statement  Box No. VII Certain documents cited  Box No. VII Certain defects in the infernational application  Box No. VIII Certain observations on the international application  2. FURTHER ACTION  If a decand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPRA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPPA and the chosen IPPA has notified the International Bureau under Rule 66.1btr(b) that written opinions of this International Searching Authority will not be so considered.  If this opinion is, as provided above, considered to be a written opinion of the IPRA, the applicant is invited to submit to the IPRA writen opinion of the IPRA, the applicant is invited to submit to the IPRA writen erply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.  For further options, see Form PCT/ISA/220.	GIULIO A. DECONTI				PC FEC'D 2 0 MAY 2005					
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3. For further details, see notes to Form PCT/ISA/220.	IPEA of Fo	a written reply to mn PCT/ISA/220	ogether, when or before the	re appropriate, with amend expiration of 22 months fi	iments, before the ex	piration of 3 months from the date of mailing				
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Alexandra, Virginia 22313-1430  Facsimile No. (703) 305-3230  Form PCI/ISA/237 (cover sheet) (January 2004)	Facsimile ]	No. (703) 305-32	30		Telephone No. 5	71-2/3-8300				

## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International	application No	).

PCT/US04/36641

Box No. 1. Basis of this opinion						
1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.						
This opinion has been established on the basis of a translation from the original language into the following language, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).						
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:						
a. type of material						
a sequence listing						
table(s) related to the sequence listing						
b. format of material						
in written format						
in computer readable form						
c. time of filing/furnishing						
contained in international application as filed.						
filed together with the international application in computer readable form.						
furnished subsequently to this Authority for the purposes of search.						
In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or famished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.						
4. Additional comments:						
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Form PCT/ISA/237(Box No. I) (January 2004)						

## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No. PCT/US04/36641

INTERNATIONAL SCARCING	AUIROKILI								
Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement									
1. Statement									
Novelty (N)	Claims 1-45,	54	YBS						
	Claims <u>46-53</u>		NO						
Inventive step (IS)	Claims 1-17,	19-45, 54	YES						
	Claims 18, 46	j-53	NO						
Industrial applicability (IA)	Claims 1-54		YES						
, ,	Claims NON	8	NO						
•			•						
2. Citations and explanations:  Claims 46-53 lack rovelty under PCT Article 33(2) as being articipated by Allen et al.  Allen et al. disclose a transgenic mouse having disruption in the endogenous KRC gene by deletion of a portion of said gene (see page 289, Figure 1 and text). Therefore, Allen et al. discloses the instantly claimed invention.  Claims 18 lack an inventive step under PCT Article 33(3) as being obvious over Allen et al. Allen et al. discloses cells with KRC disruption. It is obvious to use said cells to find modulators that modulates KRC activity.  Claims 1-17, 19-45 and 54 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest a method of identifying a compound which modulates the interaction between KRC and Jun, GATA3, SMAD or Runz2, method for inhibiting neoplasia by contacting the subject with said modulator, and a transgenic animal deficient in KRC with the claimed phenotype.  Claims 1-54 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.									